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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,048	12/27/2001	Ernst Heinz	0093/000032	5170

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NOVAK DRUCE DELUCA & QUIGG, LLP
1300 EYE STREET NW
SUITE 1000 WEST TOWER
WASHINGTON, DC 20005

EXAMINER	
GUZO, DAVID	

ART UNIT	PAPER NUMBER
1636	

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06/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/019,048	HEINZ ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *11-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *2/28/07*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

35 USC 112, 1st Paragraph Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is necessitated by applicants' amendment filed 3/12/07.

Initially, it is noted that the previous 35 USC 112, 1st paragraph (Written description) rejection against claims 1-10 is withdrawn. An examination of the prior art reveals that the structures of Δ6-desaturase enzymes were well known. Conserved regions essential for Δ6-desaturase activity (i.e. histidine boxes, cytochrome b_5 domains, etc.) were known and a reasonable structure-function relationship between the structure of Δ6-desaturase molecules and their enzymatic activity was disclosed in the prior art. Given that a reasonable structure-function relationship was known for Δ6-desaturase enzymes, the skilled artisan would be able to generate molecules with the recited level of sequence homology to SEQ ID NO:2, wherein said molecules would retain some or all of the enzymatic activity of the enzyme comprising the original sequence (SEQ ID NO:2).

However, a written description rejection is newly applied to new claims 16-17. Claims 16-17 read on nucleic acids at least 90% homologous to the complement of SEQ ID NO:1 (encoding the protein of SEQ ID NO:2) and which have not less than 110% or 130% of the enzymatic activity of SEQ ID NO:2. The claims therefore read on a genus of nucleic acid molecules engineered to encode Δ6-desaturase enzymes with **enhanced enzymatic activities** compared to the starting enzyme molecule (SEQ ID NO:2).

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention.

In the instant case, applicants provide no examples of nucleic acid molecules with the desired enhanced enzymatic activities. Applicants present no disclosure on how the skilled artisan would modify the sequence of SEQ ID NO:1 so as to generate a sequence encoding an enhanced Δ6-desaturase enzyme. Neither applicants nor the prior art present a structure-function relationship sufficient to allow the skilled artisan to modify a Δ6-desaturase enzyme so as to **enhance the enzymatic activity** of the enzyme. While conserved regions and motifs believed to be involved in enzymatic activity have been identified in Δ6-desaturase enzymes, neither applicants nor the prior

art teach the specific amino acid residue changes which are necessary to **improve the enzymatic activity of the enzyme**. The prior art teaches that protein engineering to improve the activity of enzymes often requires X-ray crystallography studies which elucidate the precise three dimensional structure of the enzyme so that empirical rational design techniques can be used to alter specific residues followed by testing to determine whether the change improves enzyme activity (See for example, Pohl et al., J. Biotech., 2006, Vol. 124, pp. 26-40). Applicants provide no disclosure of what the sequence(s) of a Δ6-desaturase having not less than 110% or not less than 130% of the activity of SEQ ID NO:2 would look like. Applicants claim the nucleic acid molecules by function only (i.e. level of enzymatic activity) without any relationship between structure and function. This is not sufficient to describe the claimed nucleic acids. As noted in MPEP 2163:

> A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. See also *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)). An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.").

Given the lack of any species of the disclosed invention and the lack of any structure-function relationship between the structure of the enhanced Δ6-desaturase and it function, it must be considered that the skilled artisan would conclude that applicants were not in possession of the claimed nucleic acids.

Claims 1-4 and 7-8 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for expressing the recited Δ6-desaturases (i.e. a nucleic acid sequence having the sequence shown in SEQ ID NO: 1, nucleic acid sequences which, as a result of the degeneracy of the genetic code, are derived from the sequence shown in SEQ ID NO:1, and a derivative of the nucleic acid sequence shown in SEQ ID NO: 1 which encode polypeptides with the amino acid sequence shown in SEQ ID NO: 2 and has at least 95% homology at the amino acid level without substantially reducing the Δ6-desaturase enzymatic activity of the polypeptides) in plants, alga, fungi or bacteria, does not reasonably provide enablement for expression of the recited Δ6-desaturases in animals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is maintained for reasons outlined in the previous Office Action (Mailed 10/7/05) and for reasons outlined below.

Initially, it is noted that the portion of the enablement rejection pertaining to lack of enablement for nucleic acid sequences encoding proteins at least 95% homologous to SEQ ID NO:2 is withdrawn. Applicants' arguments directed to this portion of the

rejection are therefore moot and will not be addressed. The enablement rejection **is maintained as it pertains to a process of preparing an unsaturated fatty acid in an animal wherein said animal contains at least 1 mol% of unsaturated fatty acid or contains at least 5% by weight of unsaturated fatty acids based upon the total fatty acid content in the organism**.

Applicants traverse this rejection by asserting that the term "animal" refers to animal cells (directing the examiner's attention to p. 3, lines 34-37 of the instant specification) and hence the skilled artisan would understand that they were not contemplating culturing whole animals and expressing the recited Δ6-desaturase enzymes in whole animals. Applicants assert that the skilled artisan would understand that a whole animal cannot be cultured in the sense of the claimed invention and that said skilled artisan would understand, in light of the specification, that a whole animal is not cultured. Applicants indicate that the examiner has misinterpreted the claim language to read on expressing the Δ6-desaturase enzymes in whole animals and bases his rejection on the lack of enablement for expressing the enzyme in whole animals at the recited levels. Applicants cite prior art references teachings the routine nature of transforming animal cells in culture and expressing foreign genes in said cells.

Applicant's arguments filed 3/12/07 have been fully considered but they are not persuasive. Applicants are basing their traverse of the rejection upon the assumption that the claims read on expressing the Δ6-desaturase enzymes in animal cells and not in whole animals and that the examiner has incorrectly read the claims to encompass

expression in whole animals. Initially, it is noted that the specification does recite "culturing" whole animals. The instant specification on page 3, lines 34-37 recites:

"[C]ulturing this organism means both growing plants and culturing eukaryotic or prokaryotic microorganisms such as bacteria, yeasts, fungi, ciliates, algae, cyanobacteria, animal or plant cells or cell associations, **or rearing animals** (emphasis added)."

Clearly, applicants, in the instant specification, indicate that "culturing this organism" reads on rearing whole animals and therefore, the claims do encompass a process for preparing unsaturated fatty acids at the recited levels, said process comprising expressing the Δ6-desaturase enzymes **in whole animals**.

The rejection is therefore maintained.

35 USC 112, 2nd Paragraph Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 and 13-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 9 (and dependent claims) are vague in that applicant claim a derivative of the nucleic acid sequence of SEQ ID NO:1 "[w]hich encodes the polypeptide shown in SEQ ID NO:2" ***and*** has "[a]t least 95% homology at the amino acid level without substantially reducing the Δ6-desaturase activity of the polypeptide".

It is unclear how a nucleic acid sequence can encode the precise amino acid sequence of SEQ ID NO:2 ***and*** any additional amino acid sequences which have at least 95% homology at the amino acid level to SEQ ID NO:2.

Claims 14-17 are vague in that applicants recite an isolated nucleic acid which is at least 90% homologous to SEQ ID NO:1 "and has not less than" a recited level of enzyme activity of SEQ ID NO:2. It is unclear how a nucleic acid sequence can have a percentage of the enzymatic activity of a protein (SEQ ID NO:2). A nucleic acid is not a polypeptide. It appears that applicants mean to recite a nucleic acid which is at least 90% homologous to SEQ ID NO:1 **and encodes a polypeptide** having not less than the recited level of enzyme activity of SEQ ID NO:2.

Sequence Rules Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicants, in the response filed 7/28/06, neglected to include an amendment to the specification specifically directing entry of the paper copy of the Sequence Listing into the application. Applicants, in response to this Office Action, are required to submit a paper copy of the Sequence Listing and an amendment directing it's entry into the specification.

Any rejection not repeated in this Office Action is withdrawn.

No Claims are allowed.

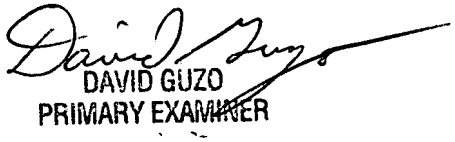
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D., can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David Guzo
May 21, 2007